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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/533,341	03/23/2000	Anna P. Catania	252/029	9950

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EXAMINER	
PARKIN, JEFFREY S	18

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 03/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/533,341	CATANIA, A., ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communicati n appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *1-12 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13 and 15-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *37 CFR 1.821 Letter* .

09/533,341

Application No.: 09/533,341

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: _____

Applicant Must Provide:

☒ An initial ~~or substitute~~ computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial ~~or substitute~~ paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE

Detailed Office Action

37 C.F.R. § 1.114

1. A request for continued examination under 37 C.F.R. § 1.114, including the fee set forth in 37 C.F.R. § 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R. § 1.114, and the fee set forth in 37 C.F.R. § 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R. § 1.114. Applicants' submission filed on 06 January, 2003, has been entered.

Status of the Claims

2. Claims 13, 15-18, and 20-23 were amended and new claims 24-33 submitted in the amendment. Claims 1-12 and 14 stand withdrawn from further consideration by the examiner, pursuant to 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention. Claims 13 and 15-33 are currently under examination.

37 C.F.R. §§ 1.821-1.825

3. This application clearly fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825. Applicants' attention is directed to the final rulemaking notice published at 55 F.R. 18230 (01 May, 1990) and 1114 O.G. 29 (15 May, 1990). If the effective filing date is on or after 01 July, 1998, see the final rulemaking notice published at 63 F.R. 29620 (01 June, 1998) and 1211 O.G. 82 (23 June, 1998). If the effective filing date is on or after 08 September, 2000, see the final rulemaking notice published in the Federal Register at 65 F.R. 54604 (08 September, 2000) and 1238 O.G. 145 (19 September, 2000). Applicant must provide an initial computer readable form (CRF) copy of the "Sequence Listing", an initial paper copy or compact disk copy of the "Sequence Listing",

as well as, an amendment directing its entry into the application. Applicant must also provide a statement that the content of the sequence listing information recorded in the computer readable form is identical to the written (on paper or compact disc) sequence listing and, where applicable, includes no new matter as required by 37 C.F.R. §§ 1.821(e), 1.821(f), 1.821(g), 1.825(b), and 1.825(d). Applicant must also amend the specification where appropriate to include the requisite sequence identifiers (e.g., see p. 12). If applicant desires the sequence listing in the instant application to be identical with that of another application on file in the United States Patent and Trademark Office, such request in accordance with 37 C.F.R. § 1.821(e) may be submitted in lieu of a new CRF.

35 U.S.C. § 112, Second Paragraph

4. Claims 13 and 15-33 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims involve the administration of "a KPV" or "a KPV composition" which is vague and indefinite since the precise metes and bounds of the patent protection desired are not readily manifest. The claim language fails to clearly set forth the salient characteristics of the compound being administered. For instance, are the applicants administering a tripeptide consisting of the amino acid sequence NH_2-Lys-Pro-Val-COOH to the patient? Alternatively, do the claims encompass the administration of a larger polypeptide that merely comprises the KPV tripeptide? Do the claims entail the administration of KPV derivatives? The precise structural features of the compound need to be clearly set forth in the claim language. It is noted that the disclosure describes experiments involving the administration of a tripeptide consisting of the amino acid sequence NH_2-Lys-Pro-Val-COOH. Appropriate amendment of the claim language is required.

Applicants' arguments and amendment fail to overcome this defect.

5. Claims 13 and 15-23 are also rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are directed toward the treatment of "secondary infections" in an HIV-infected individual. The precise metes and bounds of these limitations are not readily manifest. The clinical sequelae associated with HIV infection, including the development of opportunistic infections, is complicated and includes many symptoms (e.g., fever, pharyngitis, rash, myalgias, arthralgias, diarrhea, headache, nausea/vomiting, thrush, altered mental states, dysasthesias, and weight-loss are common problems). Are the claims directed toward a particular symptom? The disclosure discusses the antibacterial properties of KPV-containing peptides, not the treatment of any particular clinical symptom. Applicants may wish to amend the claim language accordingly (i.e., A method for inhibiting bacterial or fungal infections in an HIV-1-infected patient ... by administering to said infected patient a pharmaceutical composition comprising a polypeptide consisting of the amino acid sequence NH_2-Lys-Pro-Val-COOH ...).

6. Claims 24-33 are also rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are directed toward a method for "enhancing the killing of a pathogen" in an HIV-infected individual which is confusing. It is not readily manifest how the claimed methodology "enhances" the killing of any given pathogen. Is the claimed composition administered with another known antibacterial compound thereby resulting in some sort of synergistic effect? How does the "enhancement" take place? As set forth in the preceding

paragraph, the disclosure discusses the antibacterial properties of KPV-containing peptides, not the enhancement of pathogen killing. Applicants may wish to amend the claim language accordingly (i.e., A method for inhibiting bacterial or fungal infections in an HIV-1-infected patient ... by administering to said infected patient a pharmaceutical composition comprising a polypeptide consisting of the amino acid sequence NH_2-Lys-Pro-Val-COOH ...).

7. Claims 13, 15-18, and 20-33 are further rejected under 35 U.S.C. § 112, second paragraph, as being vague and indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the claims are incomplete for omitting essential positive methods steps, such omission amounting to a gap between the steps (refer to M.P.E.P. § 2173.05(q)). *Ex parte Erlich*, 3 U.S.P.Q.2d 1011 (Bd. Pat. App. & Inter. 1986). The claims remain incomplete and fail to include all the salient steps that are necessary to perform the claimed methodology. The claims simply state that a "KPV" composition is administered to a patient. However, the claims fail to set forth any steps pertaining to the routes of administration, administration regimen, and appropriate steps that are used to assess the effectiveness of the treatment. Applicants' arguments and amendment fail to overcome this deficiency.

35 U.S.C. § 112, First Paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 13 and 15-33 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). The claims are broadly directed toward the treatment of secondary infections in HIV-infected individuals or enhancing the killing of pathogens in HIV-infected individuals. The disclosure describes an antibacterial effect associated with the administration of a tripeptide, designated KPV, in an *in vitro* tissue culture setting. Specifically, the disclosure appears to demonstrate that KPV displays antibacterial activity toward two particular microorganisms, *Staphylococcus aureus* and *Candidia albicans*. S. *aureus* is a gram-positive bacterium while C. *albicans* is a yeast. Both microorganisms are associated with secondary or opportunistic infections in HIV-infected patients. However, the claims are broadly directed toward the treatment of any given condition and the inhibition of any given pathogen. The specification fails to provide adequate support for this claim language.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Vas-Cath, Inc., v. Mahurkar*, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). The claimed invention as a whole may not be

adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the biomolecule of interest. *In re Bell*, 991 F.2d 781, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993). *In re Deuel*, 51 F.3d 1552, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995). A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 U.S.P.Q.2d 1895, 1905 (Fed. Cir. 1995). The court noted in this decision that a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not reasonably lead those skilled in the art to any particular species.

An applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. For some biomolecules, examples of identifying characteristics include a nucleotide or amino acid

sequence, chemical structure, binding affinity, binding specificity, and molecular weight. The written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. Without such a correlation, the capability to recognize or understand the structure form the mere recitation of function and minimal structure is highly unlikely. In the latter case, disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement. *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1566, 43 U.S.P.Q.2d 1398, 1404, 1406 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998). *In re Wilder*, 736 F.2d 1516, 1521, 222 U.S.P.Q. 369, 372-3 (Fed. Cir. 1984). Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

The disclosure fails to provide adequate support for the inhibition of all other opportunistic and secondary pathogens. HIV-infected patients suffer from a number of opportunistic infections caused by any one of a number of different protozoa, fungi, bacteria, viruses, helminths, and arthropods including the herpes simplex viruses, varicella zoster virus, papilloma viruses, hepatitis viruses, poxviruses, cytomegalovirus, *Pneumocystis carinii*, *Toxoplasma gondii*, *Cryptosporidium*, *Giardia lamblia*, *Acanthamoeba*, *Candida albicans*, *Cryptococcus neoformans*, *Coccidioides immitis*, *Trichophytum rubrum*, *Staphylococcus aureus*, *Mycobacterium avium*, *Lysteria monocytogenes*, and *Treponema pallidum* (Macher *et al.*, 1988; Saag, 1997). However, the disclosure fails to address or discuss the various "pathogens" that are associated

with secondary infections during the development of AIDS. Thus, the only interest expressed appears to be directed toward the two species described in the specification, S. *aureus* and C. *albicans*. It does not appear that the inventors contemplated administering KPV tripeptides to treat any other opportunistic infection.

35 U.S.C. § 103(a)

10. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

12. The criteria that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are set forth

in *Graham et al. v. John Deere Company of Kansas City et al.; Calmar, Inc. v. Cook Chemical Company; Colgate-Palmolive Company v. Same*, 148 U.S.P.Q. 459 (U.S. Sup. Ct. 1966). These factual inquiries can be summarized as follows: 1) Determining the scope and contents of the prior art. 2) Ascertaining the differences between the prior art and the claims at issue. 3) Resolving the level of ordinary skill in the pertinent art. 4) Considering objective evidence present in the application indicating obviousness or unobviousness (i.e., commercial success, long felt but unsolved needs, failure of others, etc.).

13. Claims 13 and 15-23 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lipton (1992) in view of Saag (1997). As previously set forth, Lipton teaches that tripeptides bearing the amino acid sequence KPV are efficient **antipyretic** or anti-inflammatory compounds (see Abstract). The inventors reported (see col. 1, lines 19-24) that "**This invention relates to a new pharmaceutical composition useful for the treatment of pyrexia** and inflammation. More particularly, **this invention relates to a tripeptide sequence contained in alpha-Melanocyte Stimulating Hormone and ACTH which has been identified as an antipyretic** and anti-inflammatory agent." It was further reported (see col. 2, lines 11-23) that "**Studies comparing the antipyretic activity of centrally-administered alpha MSH to the widely-used antipyretic, acetaminophen indicate that alpha MSH is much more potent in reducing fever than acetaminophen, and that alpha MSH was more than 2500 times more potent by weight than acetaminophen in reducing fever.**" The authors also stated (col. 2, lines 25-35) that "**the shorter alpha MSH molecule, which is derived from ACTH, does not stimulate steroid release and there appears to be no irreversible deleterious effects when given to rabbits or man.**" The inventors continue in the same column and emphasize that the invention is

directed toward **amino acids 11-13 of the peptide which consists of Lys-Pro-Val, or KPV.** The inventors again note (see col. 2, lines 49-60) that "**The present invention provides a pharmaceutical composition useful in the treatment of pyrexia** and inflammation." Various well-known pharmaceutical formulations are described including compositions comprising buffers, diluents, stabilizers, and carriers (see col. 6, first and second paragraphs). Appropriate dosages are also provided, as well as, routes of administration. The only limitation of this reference is that it does not disclose the administration of this compound to HIV-infected patients. Saag (1997) reviews the clinical sequelae associated with HIV-1 infection. The author reports (p. 207, left col.) that during the intermediate stages of disease when opportunistic infections present that "Among patients with symptoms, recurrent herpes simplex infection, varicella zoster virus infection (ie, shingles), recurrent diarrhea, **intermittent fever**, unexplained weight loss, and mild oropharyngeal and vaginal candidiasis represent the **usual** manifestations of illness at this stage." Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to treat HIV-infected patients suffering from secondary infections and fever, as taught by Saag (1997), with the compounds of Lipton (1992), since this would reduce the fever and swelling associated with such opportunistic infections.

Applicants traverse and submit that there is no evidence that HIV-infected individuals suffering from secondary infections also suffer from fever. It was further argued that there is no motivation or evidence to suggest that an efficient antipyretic would also display antipathogenic properties and prove useful in limiting pathogenic growth. Applicants' arguments are clearly untenable in view of the prior art. The prior art unequivocally demonstrates that HIV-1-infected patients are routinely subject to

opportunistic infections and one of the attendant effects of that infection is fever. The prior art unequivocally demonstrates that KPV-containing peptides are efficient antipyretics. Thus, both the motivation and a reasonable expectation of success are present in the prior art.

As previously set forth, it is well-known in the prior art that bacterial and viral infections are often associated with pyretic responses. HIV-infected patients suffer from recurring bouts of secondary infections with a number of bacterial, viral, and fungal microorganisms. **These infections often result in pyretic responses.** Therefore, **there is more than sufficient motivation to administer these peptides to HIV-infected individuals particularly in light of the tremendous antipyretic properties of KPV containing compositions.** Applicants further argue that Lipton ('023) fails to describe the anti-pathogenic properties of KPV containing compounds. **Applicants are reminded that no such claim limitation is present.** The claims simply stipulate a method for treating secondary infections in HIV-infected individuals. There is no requirement that the compounds be antimicrobial in nature. Thus, if an HIV-infected patient is suffering from a fever due to a bacterial infection, there is sufficient motivation and a reasonable expectation of success in the prior art that administration of a KPV-containing compound will reduce the fever thereby ameliorating one of the symptoms associated with the secondary infection. This clearly meets all of the claimed limitations pertaining to the treatment of secondary infections. Applicants additionally argue that the anti-inflammatory properties, as they relate to hydrocortisone, would preclude the administration of this compound to HIV-infected patients, presumably because hydrocortisone suppresses the immune system. Applicants appear to have ignored the inventor's statement (col. 2, second paragraph) that "**the shorter alpha MSH molecule, which is**

derived from ACTH, does not stimulate steroid release and there appears to be no irreversible deleterious effects when given to rabbits or to man." Moreover, while KPV-containing compounds and hydrocortisone may share some common properties, nevertheless, **they are structurally and functionally different compounds that exert their effects through different pathways and mediators.** Moreover, it has been well-documented in HIV infection that proinflammatory cytokines contribute to disease progression by keeping the immune system in an activated state. Thus, one of ordinary skill in the art would have been motivated to administer KPV-containing compositions to HIV-infected patients to treat both the fever, and hyperactive immune state, of HIV-infected patients.

Correspondence

14. Correspondence related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Official communications should be directed toward one of the following Group 1600 fax numbers: (703) 308-4242 or (703) 305-3014. Informal communications may be submitted directly to the Examiner through the following fax number: (703) 308-4426. Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

15. Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (703) 308-2227. The examiner can normally be reached Monday through Thursday from 8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, James Housel or Laurie Scheiner, can be reached at (703) 308-4027 or (703) 308-1122,

respectively. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

17 March, 2003